

another penicillin. An urticarial reaction to ampicillin is more likely to be an allergic reaction. Further administration of any penicillin should be avoided unless penicillin sensitivity can be disproved.

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Rational Use of Oral Theophylline in the Treatment of Chronic Asthma

THEOPHYLLINE has been used effectively in the clinical management of chronic bronchial asthma for nearly 40 years. Until recently, however, the value of oral theophylline preparations has been controversial because of variable dose-response relationships and reports of severe and sometimes unpredictable toxicity.

Theophylline is thought to produce bronchodilatation by inhibiting the enzyme (phosphodiesterase) responsible for the conversion of cyclic adenosine monophosphate (CAMP) to 5' adenosine monophosphate (AMP). This results in higher levels of CAMP which promotes smooth muscle relaxation and prevents release of chemical mediators from the mast cell and basophil.

Recent pharmacokinetic studies of theophylline have provided information necessary for a more rational approach in the dose scheduling of this drug. Theophylline is metabolized almost entirely in the liver (10 percent is excreted unchanged by the kidney). The rate of metabolism, however, varies considerably between subjects, resulting in a rather broad range of plasma half-lives. Plasma concentrations between 10 and 20 micrograms (μg) per ml appear to provide optimal therapeutic effect; but when the concentration exceeds 20 μg per ml, the chances of having adverse side effects are increased.

The narrow margin of safety between therapeutic and toxic blood levels, and the intersubject variability of plasma half lives demand individualized dosing schedules if optimal response is to be obtained without adverse effects.

For oral theophylline therapy we suggest using USP aminophylline tablets or one of several theo-

phylline elixir equivalents. A reasonable starting dose would be 4 mg per kg of body weight per dose on a schedule of every six hours. Based on clinical response, adverse effects and plasma theophylline levels, the dose and schedule can be adjusted to achieve optimal clinical response with minimal adverse effects. When necessary a sympathomimetic drug, ephedrine or metaproterenol could be added in appropriate dosage if the patient's asthma is not controlled on theophylline alone.

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Recent Advances in Diagnosis and Treatment of Hymenoptera Hypersensitivity

ANAPHYLACTIC REACTIONS from stinging insects of the order Hymenoptera—particularly the honey bee, hornet, wasp, yellow jacket and fire ant—are a serious medical problem. The diagnosis of Hymenoptera hypersensitivity is based essentially on a clinical history, while skin testing is mainly confirmatory and used to determine the antigen dilution for the initiation of immunotherapy (hyposensitization). The preparations presently approved for both testing and treatment are commercially available whole body extracts (WBE) of insects. Reported clinical results of immunotherapy using these extracts are excellent as data from the American Academy of Allergy Insect Committee Registry have shown that over 95 percent of treated persons had either no reaction or much milder reaction when subsequently restung.

There is conflicting evidence in the literature regarding the correlation of skin test reactivity and the severity of the reactions to stings. There is also considerable overlap in the concentration of WBE which will induce positive skin tests in sensitive and nonsensitive persons. This warrants the search for more sensitive diagnostic tests and more relevant antigens for testing and treatment.

Recent *in vitro* studies using histamine release

from basophil leukocytes of hymenoptera sensitive patients using either WBE or pure venom have shown that while skin test reactivity to WBE correlated significantly with cell sensitivity in the most sensitive patients, the *in vitro* test using venom antigens could clearly distinguish sensitive persons from normals and suggests the superiority of venom antigens to WBE in this diagnostic system.

Two isolated case reports also suggest that venom antigens may be superior to WBE in the prophylactic immunotherapy of anaphylactic bee stinging reactions.

Fractionation of bee venom in several laboratories strongly suggests that phospholipase A (PLA) is one of the major allergenic components which may not be present in detectable amounts in WBE.

A radioimmunoassay (RAST) appears a promising diagnostic *in vitro* test for the detection of immunoglobulin E (IgE) antibodies to venom and phospholipase A in the sera of hymenoptera sensitive patients.

While these findings are still experimental they may serve as a basis for a more specific approach to the improved diagnosis and treatment of Hymenoptera hypersensitivity. Isolated venoms are not currently available. In the meantime, whole body extract is recommended for therapy.

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Can Food Allergy Cause Asthma?

WHILE INHALANT ALLERGY (to pollens, house dust, molds, animal danders, and the like) is generally recognized as a frequent cause of asthma, food allergy of the delayed onset type is not. A substantial number of physicians, including some allergists, doubt the importance or even the existence of this type of food intolerance. However, there is steadily increasing acceptance of its importance, its frequency, its allergic nature and its association with asthma and the tension-fatigue (allergic toxemia) syndrome.

An important reason for failure to recognize delayed onset food allergy is the fact that in such allergy, results of skin tests are usually negative for the offending food or foods. Only in the immediate onset type of food allergy, in which symptoms appear soon after ingestion, are skin tests reliable. This type of food allergy, however, is usually well known to the patient before he comes to the physician, in which case such tests only confirm what is already known. In delayed onset food allergy symptoms do not appear for several hours after ingestion. This, plus the negative reactions to skin tests combine to make recognition of this type of food allergy difficult. Another characteristic is its tendency in some patients to be manifest chiefly in winter, while almost disappearing in summer. This adds further confusion.

A patient may like an offending food and not suspect it at all or believe he tolerates it well except on certain occasions, or in large amounts or in a certain form. An offending food is usually one which is eaten frequently such as milk (including cheese, yogurt, ice cream and sherbet), chocolate (including cola drinks) or corn (including corn sugar, dextrose, corn starch, popcorn and corn oil).

Delayed-onset food allergy and inhalant allergy often coexist. A frequent reason for a less than satisfactory result in treating inhalant allergy is nonrecognition of such a coexistence.

There are no laboratory tests—including the radioimmunoassay test (RAST)—or combination of tests presently available that are reliable in diagnosing delayed onset food allergy. Diagnosis is made by trial elimination diets. Diet directions should always be given to the patient in writing and should be adhered to for a test period of at least three weeks. The trial should be supervised preferably by a physician who has followed the diet himself for a minimum of 24 hours in order to be aware of the numerous errors that may occur.

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